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ETIOLOGY AND PATHOGENESIS OF UTERINE LEIOMYOMAS: A REVIEW

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Running Title: Review of Uterine Leiomyoma

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Abbreviations:

RR – relative risk; BMI – body mass index

SERMS – selective estrogen-receptor modulators

E_1 – estrone

HRT – hormone-replacement therapy

GnRH – gonadotropin-releasing hormone

LHRH – luteinizing hormone-releasing hormone

DDT – dichlorodiphenyltrichloroethane

HPTE – 2,2-bis- (*p*-hydroxyphenyl)-1,1,1-trichloroethane

ERα - estrogen receptor alpha; ERβ - estrogen receptor beta

ESR2 – estrogen receptor beta gene

G6PD – glucose-6-phosphate dehydrogenase

PCR – polymerase chain reaction

HMGIC (now designated *HMGA2*) and *HMGIY* (now designated *HMGA1*)– high-mobility group proteins

RAD51 – recombination repair gene family

RAD51L1 (formerly *RAD51B*) – radiation-inducible gene; member of *RAD51* family

cM – centiMorgan

t – translocation; del – deletion; inv – inversion; ins – insertion; q – long arm of chromosome; p – short arm of chromosome

PR – progesterone receptor

TGF-β - transforming growth factor beta; bFGF – basic fibroblast growth factor

EGF – epidermal growth factor; PDGF – platelet-derived growth factor

VEGF – vascular endothelial growth factor; IGF – insulin-like growth factor

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Abstract

Uterine leiomyomas, or “fibroids”, represent a major public health problem. These tumors probably develop in the majority of American women and become symptomatic in one third of these women. They are the most common cause of hysterectomy in the United States. Although the initiator(s) of fibroids are unknown, several predisposing factors have been identified, including age (late reproductive years), African-American ethnicity, nulliparity, and obesity. Non-random cytogenetic abnormalities have been found in about 40% of tumors examined. Estrogen and progesterone are recognized as promoters of tumor growth, and the potential role of environmental estrogens has only recently been explored. Growth factors with mitogenic activity, such as $TGF\beta_{3,}$ bFGF, EGF, and IGF-I, are elevated in fibroids, and may be the effectors of estrogen and progesterone promotion. These data offer clues to the etiology and pathogenesis of this common condition, which we have analyzed and summarized in this review.